UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

April 21, 2015

MEMORANDUM

Subject: Acute Toxicity Review for EPA File Symbol 1677-ELR
Data Package 424443
Product Name: Peroxide Disinfectant and Glass Cleaner RTU

From: Wallace Powell, Biologist
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To: John Hebert, PM 33/ Terria Northern
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: Ecolab Inc.

FORMULATION FROM PROPOSED LABEL:

Active Ingredient:	% by weight
Hydrogen Peroxide (EPA PC Code 000595)	0.39
Other Ingredient(s):	99.61
Total:	100.00

BACKGROUND

In support of registration for the subject product, Peroxide Disinfectant and Glass Cleaner RTU, the applicant has cited studies to support the requirements for acute oral, acute dermal, and acute inhalation toxicity, and eye and skin irritation, and has submitted a study for dermal sensitization.

DISCUSSION AND RECOMMENDATION

Acute oral toxicity, acute dermal toxicity

The applicant has cited MRID 49253301 for acute oral toxicity and 49253302 for acute dermal toxicity. Those documents were previously submitted under EPA Reg. No. 1677-238. The documents reference an acute oral toxicity study of MRID 48947442 and an acute dermal toxicity study of MRID 48947441. These two studies were accepted and assigned Toxicity Category III for Reg. No. 1677-238 in a Product Science Branch (PSB) review of 1/24/2013 (DP 405935). Later, in a PSB review of 3/13/2014 (DP 416483), citations of these studies were accepted in support of acute oral and acute dermal toxicity Category IV for the most concentrated use-dilution of Reg. No. 1677-238. That use-dilution represents the same active-ingredient concentration as – and is substantially similar to (from an acute toxicity perspective) – Peroxide Disinfectant and Glass Cleaner RTU. Therefore, PSB recommends Category IV for Peroxide Disinfectant and Glass Cleaner RTU for acute oral and acute dermal toxicity based on MRID 48947442 and 48947441.

Acute inhalation toxicity

The applicant has submitted MRID 49488204, a discussion document. The document references an acute inhalation toxicity study of MRID 48947439. The study was accepted in support of Toxicity Category III for Reg. No. 1677-238 in a PSB review of 1/24/2013 (DP 405935). Later, in a PSB review of 3/13/2014 (DP 416483), a citation of the study was accepted in support of the same Toxicity Category (III) for the most concentrated use-dilution of Reg. No. 1677-238, an approximately 21-fold dilution (by volume, unadjusted with respect to Certified Limits). That use-dilution represents the same active ingredient concentration as – and is substantially similar to – Peroxide Disinfectant and Glass Cleaner RTU.

Therefore, assignment of acute inhalation Toxicity Category III would be indicated from the 3/13/2014 PSB review. However, the applicant has included in MRID 49488204 a request and rationale for assignment of Category IV. The rationale involves the use of Probit analysis using data from the substance tested in MRID 48947439 to extrapolate down to the dilution (using percent active ingredient as a point of comparison).

The Probit method can facilitate the evaluation of dose response for appropriately distributed data within a tested range of dose concentrations. However, the Probit method is essentially inapplicable to responses to concentrations far below that tested range.

However, the assignment of acute inhalation Toxicity Category IV does appear reasonable, in consideration of (1) the results of the MRID 48947439 study, (2) the dilution rate (approximately 21-fold by volume) represented by the subject product (Peroxide Disinfectant and Glass Cleaner RTU), and (3) the concentration of hydrogen peroxide in the subject product. PSB therefore recommends Category IV, though not on the basis of the Probit approach in the MRID 49488204 rationale.

Eye irritation, skin irritation

The applicant has cited MRID 48947443 for eye irritation and 48947444 for skin irritation. These two studies were accepted for Reg. No. 1677-238 in a PSB review of 1/24/2013 (DP 405935). They were assigned Toxicity Category III for eye irritation and IV for skin irritation. Later, in a PSB review of 3/13/2014 (DP 416483), citations of these studies were accepted in support of the

same Toxicity Categories (III for eye irritation, IV for skin irritation) for the most concentrated use-dilution of Reg. No. 1677-238. That use-dilution represents the same active-ingredient concentration as – and is substantially similar to – Peroxide Disinfectant and Glass Cleaner RTU. Therefore, PSB recommends eye irritation Category III and skin irritation Category IV, for Peroxide Disinfectant and Glass Cleaner RTU.

Skin sensitization

The applicant has submitted MRID 49488203 for dermal sensitization. The study is acceptable and is negative for sensitization. A review of the study is attached to this memorandum. The registrant's 11/11/2014 letter confirms that the test substance in the study is the same as Peroxide Disinfectant and Glass Cleaner RTU.

Summary

The acute toxicity profile of Peroxide Disinfectant and Glass Cleaner RTU is currently:

Study	MRID	Toxicity Category	Status
Acute Oral Toxicity	49253301 (cited), 48947442 (study cited in MRID 49253301)	IV	Cited
Acute Dermal Toxicity	49253302 (cited), 489474-41 (study cited in MRID 49253302)	IV	Cited
Acute Inhalation Toxicity	48947439 (study cited in MRID 49488204)	IV	Cited
Primary Eye Irritation	48947443	III	Cited
Primary Dermal Irritation	48947444	IV	Cited
Dermal Sensitization	49488203	Non-sensitizer	Acceptable

PRODUCT LABELING:

The First Aid and human-hazard precautionary statements in the proposed labeling dated 11/10/2014 are acceptable.

DATA REVIEW FOR SKIN SENSITIZATION TESTING (OPPTS 870.2600)

Product Manager: 33
MRID No.: 49488203

Reviewer: W. Powell
Study Completion Date: 10/2/2014
Report No.: MB 14-22674.06

Testing Laboratory: MB Research Laboratories
Author: Debra A. Hall

Quality Assurance (40 CFR §160): Included

Test Material:

Substance: 3 in 1 RTU – 0.4 mL
Applied 100% (neat) for both induction and challenge

Animals: Guinea pig, Hartley albino
Test group: 20 (10 per sex)
Naïve control: 10 (5 per sex)
Preliminary irritation testing: None

Historical Positive Control:

Substance: Alpha-Hexylcinnamaldehyde, 85% – 0.4 mL
Applied undiluted for induction,
50% (of the 85%) v/v in acetone for challenge

Animals: Guinea pig, Hartley albino
Test group: 20 (10 per sex)
Naïve control: 10 (5 per sex)

Method: Buehler

Summary:

1. 3 in 1 RTU did **not** appear to be a contact sensitizer.
2. **Classification**: Acceptable

Deviations from Guideline 870.2600 and other comments:

1. Room temperature range extended slightly higher than the 870.2600 Guideline. Relative humidity reached as high as 97.5% and thus exceeded the Guideline range of up to 70%. The study report states that the temperature and humidity fluctuations occurred gradually. The deviations would not be expected to affect the study outcome.

2. The report for the positive control study could have better clarified that the "100%" hexylcinnamaldehyde was 100% of the 85% technical grade.

Results:

In the main study (3 in 1 RTU), erythema observed following both induction and challenge was not significant. Erythema following challenge was reasonably comparable to the Naïve Control group. Thus, the study results indicate that 3 in 1 RTU was **not** a contact sensitizer.

The Historical Positive Control study results were appropriate, and the study was conducted within six months of the main study.

Incidence of Erythema Response at Challenge – 3 in 1 RTU

	Incidence of Positive Response[1]		Severity[2]	
	24 Hrs	**48 Hrs**	**24 Hrs**	**48 Hrs**
Test Group	1 / 20	1 / 20	0.075	0.05
Naïve Control Group	0 / 10	0 / 10	0.0	0.0

[1] Number of erythema scores of 1 or greater, per number of animals evaluated.
[2] Sum of the erythema scores divided by the number of animals evaluated.

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Skin Reaction Scores (Erythema) – 3 in 1 RTU

	Induction						Challenge	
	1		2		3			
Concentration→	100%		100%		100%		100%	
Hours after dose→	24	48	24	48	24	48	24	48
Animal No.								
Test Group								
D6244	0	0	0	0.5	0.5	0	0	0
D6245	0.5	0	0	0	0	0	0.5	0
D6246	0	0	0	0	0	0	0	0
D6247	0	0	0	0	1	0	0	0
D6248	0	0	0	0	0	0	0	0
D6249	0	0	0	0	0	0	0	0
D6250	0	0	0	0	0	0	0	0
D6251	0	0	0.5	0	0	0	1	1
D6252	0	0	0	0	0.5	0	0	0
D6253	0	0	0	0	0	0	0	0
D6254	0	0	0	0	0	0	0	0
D6255	0	0	0	0	1	0.5	0	0
D6256	0	0	0	0	0	0	0	0
D6257	0	0	0	0	0.5	0	0	0
D6258	0	0	0	0	0	0	0	0
D6259	0	0	0	0	0	0.5	0	0
D6260	0.5	0	0	0	0	0	0	0
D6261	0	0	0	0	0	0	0	0
D6262	0	0	0	0	0	0	0	0
D6263	0	0	0	0	0	0	0	0
Naïve Control Group								
D6264	—	—	—	—	—	—	0	0
D6265	—	—	—	—	—	—	0	0
D6266	—	—	—	—	—	—	0	0
D6267	—	—	—	—	—	—	0	0
D6268	—	—	—	—	—	—	0	0
D6269	—	—	—	—	—	—	0	0
D6270	—	—	—	—	—	—	0	0
D6271	—	—	—	—	—	—	0	0
D6272	—	—	—	—	—	—	0	0
D6273	—	—	—	—	—	—	0	0